IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Iris Pecker et al.

Serial No.: 09/988,113

Filed: November 19, 2001

Group Art Unit: 1652

For: POLYNUCLEOTIDE ENCODING A POLYPEPTIDE HAVING HEPARANASE ACTIVITY AND EXPRESSION OF SAME IN GENETICALLY MODIFIED CELLS

Attorney Docket: 01/22781

Examiner: R. HUTSON

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

DECLARATION OF IRIS PECKER UNDER 37 CFR 1.132

I am presently employed as researcher in Insight Strategy & Marketing Ltd. I received my Ph.D. in molecular biology degree from the Hebrew University of Jerusalem (Israel) in 1994, after which I worked as a post-doctoral fellow in the Tel Aviv University (Israel) in the field of Human Genetics. In 1996 I joined Insight and presently serve as the head of the molecular biology department, supervising the activities of 10 other workers.

I am a co-inventor of the subject matter claimed in the above-referenced U.S. patent application.

I have read the Examiner's Office Action dated November 19, 2001. I hereby declare the following.

Heparanase has a specific, well characterized and unique catalytic activity known for over 20 years. Over the years, heparanase was partially purified from a variety of mammalian sources. Heparanase is defined as a GAG hydrolase which

cleaves heparin and heparan sulfate (both are sulfated) at the beta-1,4 linkage between glucuronic acid and glucosamine. Heparanase is an endolytic enzyme and the average product length it generates is 8-12 saccharides.

The present invention represents a significant, non-obvious, inventive advance over the prior art.

The present invention encompasses polynucleotides encoding for polypeptides having a sequence of at least 70% homology to SEQ ID NO:10. Many different heparanase sequences are known, having different degrees of homology to the sequence of SEQ ID NO:10, which is a human sequence. For example, mouse B16-F10 heparanase as well as human platelet heparanases and heparanase enzymes produced by several human tumor cell lines are known. However, the mouse heparanase amino acid sequence is known to have less than 80% identity to human heparanase, as described in published PCT Application No. WO 00/52178: POLYNUCLEOTIDE ENCODING A POLYPEPTIDE HAVING HEPARANASE ACTIVITY AND EXPRESSION OF SAME IN GENETICALLY MODIFIED CELLS. Furthermore, sequence information available about a variant of the B16-F10 cell line shows that the sequence of heparanase in the cell line is apparently identical to the sequence of heparanase in normal mouse tissue. This example was already described in the present Application, for example in Figure 17. Therefore, actual experimental support (in the form of examples) is provided for heparanase sequences that have homology of less than about 80%.

To further clarify this point, Applicant has submitted alignment data in the attached Appendix, showing the homology (and differences) between human, rat, mouse and chicken heparanase sequences (part of this information has already been included in the present Application, see for example Figure 17). Some important

shared features such as active site residues and the heparin binding sites are marked. This information further supports Applicant's statements with regard to both the heparanase sequences of the present invention, and also the ability of one of ordinary skill in the art to readily recognize a heparanase protein as such.

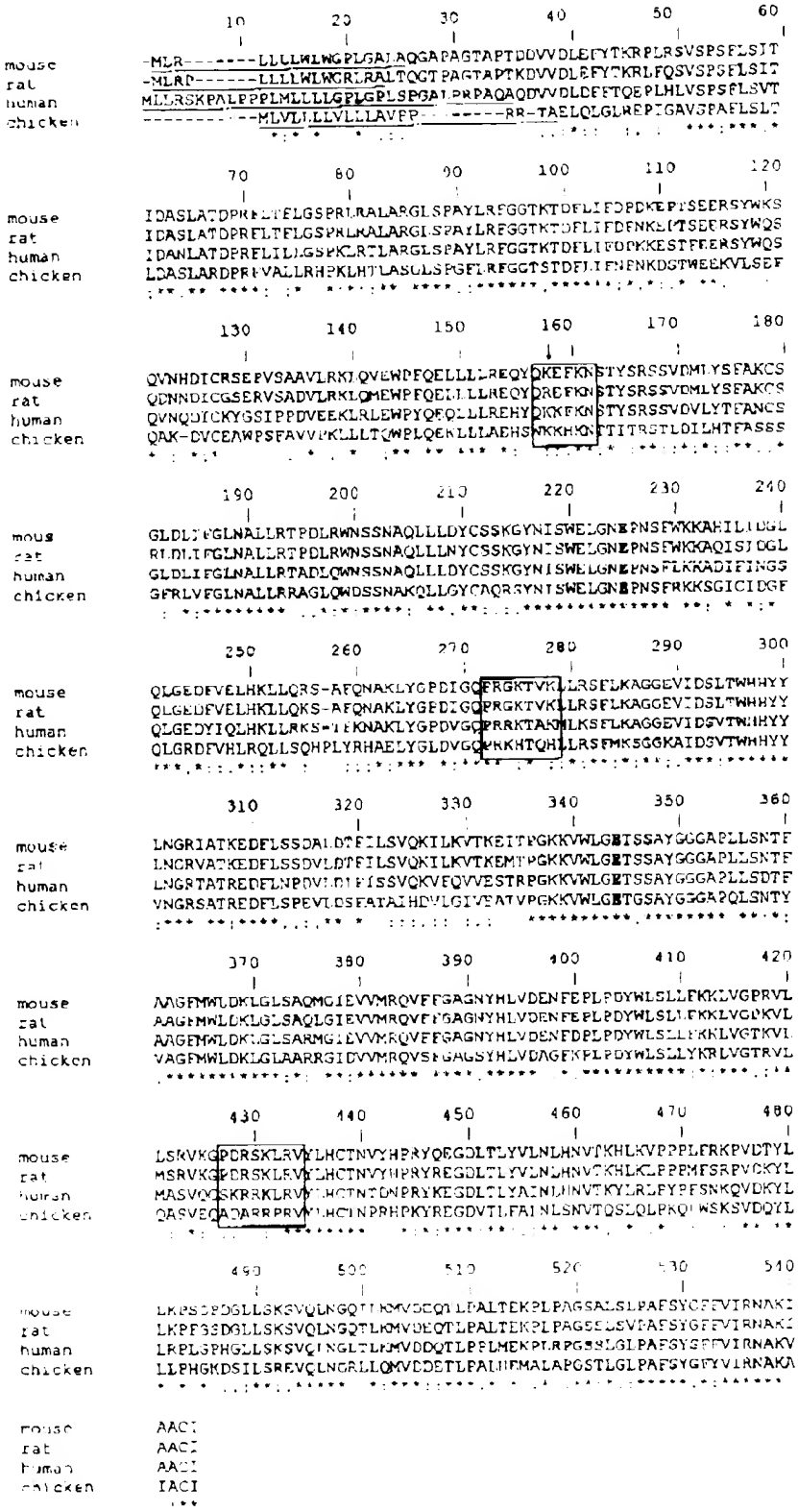
I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United states Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

August 12, 2003

Iris Pecker

Dr. Iris Pecker

APPENDIX - Sequence Homology Data



Multiple alignment of heparanase from Human, Rat, Mouse and chicken generated by Clustal W. Active site residues are bolded and putative heparin binding sites are boxed.